**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Patent Application of

**ANAND ET AL.** Atty. Ref.: **620-406**

Serial No. **10/563,042** Group: **1611**

Filed: **March 13, 2006** Examiner: **Love, Trevor M**

For: METHOD FOR INCREASING THE EFFICACY OF A MITOTIC SPINDLE ASSEMBLY INHIBITOR WITH AN AURORA KINASE INHIBITOR

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Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

**DECLARATION**

I, Ashok Venkitaraman, do hereby declare and say as follows:

1. I hold the Ursula Zoellner Professorship of Cancer Research in the Department of Oncology at Cambridge University, am Director of the Medical Research Council's Cancer Cell Unit, and have **12** years of experience in the field of cancer research. I am also one of the inventors of the invention claimed in the above-identified application.

2. I have read the Office communication dated 11 June 2010 and the documents Sen et al (1997) Oncogene 14 2195-2200; Patel et al (2000) Oncogene 19 4159-4169; Entrez Gene, Aurora kinase A; Hauf et al J. Cell Biol (2003) 161 281–294; Slamon et al (2001) N Engl J Med 344 11 783-792 and Obermiller et al Breast Cancer Res (2000) 2 28-31. I offer the following comments on the technical issues which were raised in the Office communication.

3. Paclitaxel is a well-characterised cancer drug which induces cell cycle arrest and apoptosis in cancer cells. Low doses of paclitaxel can induce ploidal variations in cells and this effect is recognised in Patel et al. However, hypodiploidy or other ploidal variations are not associated with apoptosis or cell death. This is also recognised in Patel et al on page 4164, which states:

*It was demonstrated previously that rates of paclitaxel-induced apoptosis directly correlate with number of G2/M arrested cells rather than number of hypodiploid cells*

Therefore, researchers in the field of cancer therapy would not expect the induction of hypodiploidy that is observed at low doses of paclitaxel to make any significant contribution to the anti-cancer activity of paclitaxel.

4. Hauf et al reports that Hesperadin inhibits chromosome alignment and segregation in cells. However, Hauf et al does not indicate that hesperadin increases apoptosis or cell death. Indeed, Figure 8 of Hauf et al shows that hesperadin overrides the cell cycle arrest that is induced by paclitaxel. As noted in Patel et al cited above, rates of paclitaxel-induced apoptosis correlate with paclitaxel-induced arrest. Thus, the data shown in Figure 8 of Hauf et al indicates that hesperadin should actually reduce the sensitivity of cells to taxol.

5. Based on Patel and Hauf, researchers in the field of cancer therapy would not attempt to treat cancer by administering paclitaxel and hesperadin together because they would understand from Hauf et al that hesperadin antagonises paclitaxel and negates its anti-cancer effect.

6. Not all cancers over-express Aurora-A In fact, only about 30-50% of cancers over-express Aurora-A. However the data in the specification, which was published in Anand et al (2003) Cancer Res 3 51-62 shows that the subset of cancers which over-express Aurora-A are resistant to the effect of paclitaxel.

7. It is my belief that researchers in the field of cancer therapy would not have predicted from Hauf et al, Sen et al or Patel et al that the overexpression of Aurora-A would be responsible for resistance to paclitaxel, or that Aurora A inhibitors would be useful in reducing this resistance.

8. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Signed this ___9__ day of __November___, 2010.

(Signature) _____ _____

Ashok Venkitaraman